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Surveillance imaging for high-grade childhood brain tumors: what to do ten years after completion of treatment?

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35 Abbreviation key

ATRT	Atypical teratoid rhabdoid tumor
CNS	Central nervous system
DIPG	Diffuse intrinsic pons glioma
EPN	Ependymoma
FA	Fractional anisotropy
FLAIR	Fluid attenuation inversion recovery
GBM	Glioblastoma multiforme
GTR	Gross total resection
HGG	High-grade glioma
IVM	Intracerebral vascular malformations
LGG	Low-grade glioma
MB	Medulloblastoma
MRI	Magnetic resonance imaging
PBL	Pineoblastoma
PNET	Primitive neuroectodermal tumor
SMN	Secondary malignant neoplasm
stPNET	Supratentorial primitive neuroectodermal tumor
WML	White matter lesion

36

37

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Abstract

Brain tumors are the second most common childhood cancer. Treatment protocols for high-grade pediatric brain tumors recommend regular follow-up imaging for up to ten years. We review maximal time to recurrence and minimal time to radiologically detectable long-term sequelae like secondary malignancies, vascular complications and white matter disease. No tumors recurred after the ten-year point, but radiological long-term sequelae grew more common as the treatment completion date receded. We do not recommend regular imaging more than ten years after treatment has ended, unless there are clinical symptoms.

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Introduction

Tumors of the central nervous system (CNS) are the second most common tumor in childhood after leukemia. The incidence is comparable in western countries (5.47/100,000 aged 0-14 years and 5.67/100,000 aged 0-19 years in the US, 2-4/100,000 aged 0-15 years in Germany and Switzerland)[1,2]. Advances in imaging techniques, neurosurgery, radiotherapy, chemotherapy and supportive care have increased the survival rate significantly. Five-year relative survival for all brain tumors has increased from around 60% at the end of the 1970s to around 72.5% by 2007-2013[3], though the survival rate varies between different pediatric CNS tumors. When they are cured of their primary malignancy, children need regular follow-up investigations and screenings for tumor recurrence and long-term side effects caused by chemotherapy, radiotherapy, surgery or the tumor itself. For most tumors, a national and/or international treatment protocol recommends procedures for initial diagnosis, treatment and follow up, but these recommendations usually cover only the first five or ten years after the end of treatment.

This review summarizes the most important findings detectable on imaging ten years or more after the end of treatment for pediatric high-grade brain tumors, which includes the period of possible tumor recurrence. We also summarize possible long-term sequelae visible on imaging (secondary malignant neoplasm, vascular complications, and white matter disease) caused by the treatment.

Methods

We used PubMed for the literature search. Search terms included the different biological types of high-grade brain tumors (medulloblastoma [MB], ependymoma [EPN], supratentorial primitive

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neuroectodermal tumor [stPNET], atypical teratoid rhabdoid tumor [ATRT], malignant glioma/high grade glioma [HGG] and diffuse intrinsic pons glioma [DIPG]) and the term "embryonal tumors". In addition to the single biological subtypes we combined those with the terms "surveillance imaging", "relapse", "relapse pattern", "outcome", "cavernoma", "intracerebral cavernous malformations", "intracerebral vascular malformations" (IVM), "secondary malignant neoplasm (SMN)", "secondary malignancy", "leukomalacia", "leukoencephalopathy", "white matter" and "childhood". We also screened the reference lists of the eligible publications.

Inclusion criteria for all publications are diagnosis of a high-grade brain tumor and age at first tumor diagnosis of 0-18 years. We also included publications with patient aged >18 years if the proportion of the pediatric population was described separately. An additional inclusion criterion for tumor recurrence was diagnosis after 1999; these studies have comparable and less heterogeneous treatment modalities, especially for radiotherapy. We only evaluated time to first recurrence. Secondary malignant neoplasm, intracerebral vascular malformation, and leukoencephalopathy have separate inclusion criteria for the year of first tumor diagnosis (after 1989) and year of publication (after 1999).

We excluded all publications with less than 10 patients and those where leukoencephalopathy developed during the treatment. Patients with tumor predisposition syndrome are excluded, as in this population follow-up recommendations are more complex and have to include multiple different tumor types also outside of the CNS.

Results

Tumor recurrence

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Table 1 provides an overview of the most important findings from the eligible studies on tumor recurrence.

Medulloblastoma (MB)

Medulloblastoma make up 15-30% of all brain tumors and are the second most common brain tumor after astrocytoma[4]. Around 50% develop before the age of 5 years. Initial metastatic disease is present in about one third[5,6].

Tumor recurrence rate was between 18.7%-40%. [5,7-14]. No relapse occurred more than ten years after diagnosis. The longest documented latency period was 7.9 years, in a patient with standard risk MB[7]. The proportion of late relapse, arbitrarily defined as >5 years from diagnosis, is mentioned in two publications and is 8% and 7% respectively[7,8]. According to Sabel et al. and Perreault et al. 69% and 46% of all recurrences were asymptomatic and detected by surveillance MRI[7,9,10].

Ependymoma (EPN)

EPN represent 10 % of all CNS tumors in childhood. They occur mostly in the first decade of life and more than 50% of children are aged <5 years at diagnosis. EPN present with initial leptomeningeal dissemination in 5-10% of cases[4,15,16].

30 – 54% of patients relapsed between 1 month and 8.6 years from diagnosis, with am mean of 12 to 19 month[9,17-20]. No data concerning symptomatic or asymptomatic recurrence are available.

Atypical teratoid rhabdoid tumor (ATRT)

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ATRT are rare (1-2%) brain tumor in childhood and affect predominantly infants and toddlers. About two-third of newly diagnosed ATRT occur before the age of 3 years. In 21-30%, dissemination is present at initial diagnosis[21-23].

Relapse occur in 40 – 74% of patients with a mean latency period around 5 month and the latest relapse after 3.2 years[9,24-28]. No data concerning symptomatic or asymptomatic recurrence are available.

Central nervous system primitive neuroectodermal tumors (CNS-PNET), Pineoblastoma (PBL)

CNS-PNET and PBL represent 2.5% - 4.8% and 0.6% of all CNS tumors respectively[4,29]. In the reviewed literature, initial metastatic disease was present 35% and 48% respectively [10,30].

The rate of recurrence was between 42% and 76%[10,30,31]. The latest manifestation occurred after 4.5 years in a patient with CNS-PNET[10]. No data concerning symptomatic or asymptomatic recurrence available.

High-grade glioma (HGG) and Diffuse intrinsic pons glioma (DIPG)

HGG together with DIPG represent 8 - 17% of all CNS tumors in childhood and adolescence up to 19 years of age and are responsible for a relevant part of mortality (up to 40% of all brain tumors)[4,32,33]. According to data from four consecutive German HGG protocols, about 3% have initial metastatic disease[34].

The rate of progressive disease after one year was 75% in the study from Macy et al[35]. The event free-survival after one year was higher (43%) according to Wolff et al[36]. The 5-year event-free survival in this cohort was 13%.

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Radiological long-term sequelae

Table 2 summarizes the most important findings from the eligible studies on SMN, IVM and WML.

Secondary malignant neoplasia

The median follow-up from diagnosis for the six eligible studies ranges from 1.0 to 10.0 years with a maximum of 15.0 years[7,11,37-40]. The primary diagnosis was either medulloblastoma, ependymoma or HGG/DIPG. All SMN occurred in patients after radiotherapy. Secondary brain tumors were detected in 0.1 – 4.1% of former brain tumor patients. The histology of all 19 cerebral SMN are available[7,11,37-40]. Hereof 79% are high-grade lesions (high-grade glioma and PNET), 15% are meningioma, and 5% are pilocytic astrocytoma. Time to detection of SMN is available from five studies, ranging from 2.4 years (PNET) to 10.3 years (high-grade glioma)[7,11,37-39]. Time to detection of low-grade tumors is available in two cases and is 6.5 years (pilocytic astrocytoma) and 10.2 years (meningioma) respectively[37,39]. In case of high-grade tumors (n=11) time ranges from 2.4 to 10.3 years.

Intracerebral vascular malformations

Only one study assessing radiation-induced cavernoma in medulloblastoma patients fulfilled the inclusion criteria[41]. During the observation period of mean 7.2 years, 31% developed at least one intracerebral cavernoma. The cumulative incidence rate was 5.6%, 14% and 43% 3, 5 and 10 years following radiotherapy for MB. Time to detection of a vascular malformation lied between 1.1 and 16.1 years with a median of 6.6 years. One out of 18 patients had clinical symptoms at

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diagnosis. He presented five years after treatment with seizure, headache, and emesis. All patients received radiotherapy to the brain.

Leukoencephalopathy/ White matter lesions

WML is a well-known late effect after treatment for pediatric brain tumors, either after focal irradiation or after low dose craniospinal radiotherapy and chemotherapy[42,43]. Depending on the severity, mostly studies classify WML in grade 1-3, rarely up to grade 4. Grade 1 lesions correspond to small areas with high signal in T2* and FLAIR in MRI. These lesions increase in grade 2 and become cystic or hemorrhagic in grade 3 and 4 lesions[44]. These changes can occur in parallel with an increase in subarachnoidal space and ventriculomegaly[43]. Different grades of WML can manifest in the same patient[42-45]. The incidence of WML lies between 33% and 100%[42-46]. Two studies included MB only[42,45,46]; the remaining two include more than one biological type of brain tumor[43,44]. All patients received different combinations of chemotherapy and radiotherapy. The percentage of grade 1 lesions in each study ranges from 33 to 66%. Grade II lesions and grade III lesions were visible in 7-33% and 29% respectively.

Discussion

We found no recurrence of the primary brain tumor, either local or distant, ten years or more after the end of treatment in the reviewed literature[5,7-14,18-20,24-28,30,31,35,36,47,48]. After combining the latency period from all relapses, median time to relapse was 13.7 months; average minimal latency times were 3.3 months and a maximum of 49.0 months. A patient diagnosed with ependymoma had the longest latency period (103 months). Overall, these results do not seem to

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justify routine screening to detect tumor recurrence more than ten years after the end of treatment.

Radiotherapy is a known risk factor for developing SMN in the previously irradiated field. Data from the large Childhood Cancer Survivor Study (CCSS) show that the risk for SMN in the brain increases as the diagnosis recedes. Results from large studies emphasise a linear dose-response-relationship between meningioma and glioma as SMN with a steady increase of occurrence for both tumors over time (cumulative incidence 3.3% at 25 years; 3.5% at 30 years)[49,50]. Most of the SMN in the reviewed literature are high-grade tumors. Only two studies reported occurrence of secondary meningioma[37,40]. Studies with longer follow-up periods show a larger proportion of secondary meningioma. In the CCSS cohort, the cumulative incidence of benign meningioma was 3.3% after a median follow-up of 19.6 years[51]. The latency period for SMN in the brain is very heterogeneous in the reviewed literature (2.4 to 10.3 years) and the development of SMN follows no predictable pattern. For slowly growing tumors (e.g. meningioma), the prognosis is not inferior if the tumor is diagnosed due to clinical symptoms compared to earlier detection by surveillance MRI. Data of women with newly diagnosed meningioma during pregnancy support this suggestion[52-54]. In case of absent neurological symptoms or deterioration, the management provides tight follow-up and surgery after delivery. The interval between diagnosis and surgery can thereby last up to several weeks[52-54]. To detect fast-growing secondary brain tumors (e.g. GBM) in an early stage, the interval between the scans would have to be very short. Even though the possibility is high to miss the tumor on MRI because the tumor was not visible on the previous but manifests clinically before the subsequent examination. In summary, it is not possible to recommend regular screening for early detection of SMN.

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Cavernoma occur more often in previously irradiated patients and detection rate depends on imaging techniques. The prevalence of cavernoma in the reviewed study is 31%. This prevalence is higher than in non-irradiated children and young adults with a prevalence of 0.6%[55] and also higher than in other publications including patients partially diagnosed before 1990 with rates of 3.4% and 4.2%[56,57]. Different MRI techniques could cause some of these differences. In the study from Burn et al. no T2*-weighted imaging was performed[56]. This technique is sensitive to detect blood artefacts and was used in the reviewed study. Studies including patients from past eras, not using specific MR techniques, probably underestimate the prevalence of cavernoma. Cavernoma bear the risk of spontaneous bleeding. In the study from Lew et al. 20 lesions were longitudinally followed[41]. They increased in size in 70% of cases, were stable in 15%, and a decreased in 15%. Despite an increase in size in 70% of cases, no patient suffered from acute bleeding during the follow-up period. The hemorrhage rate in non-irradiated children is 3.3% and 1.6% per patient-year respectively[55,58]. Other publications show a bleeding rate for radiation-induced cavernoma of 10%[59]. Radiation dose and time of follow-up may have an effect on the development of cavernoma. Unfortunately, the reviewed study did not comment on the possible effect of radiation dose. Cutsforth et al. showed, that patients treated with higher radiation doses had a shorter period to detection of cavernoma[59]. Burn et al. showed no correlation between radiation dose and the latency period[56]. According to Lew et al. with increasing time from end of treatment, the cumulative incidence of cavernoma increases[41]. With the knowledge of the dynamic behaviour in the natural course of cavernoma, we recommend a wait-and-see strategy with close follow-up imaging in case of an asymptomatic incidental finding. Due to the wide

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range of latency period to detection of cavernoma, no interval for regular follow-up imaging can be deduced.

A second cerebral vascular disorder observed after radiotherapy to the brain is moyamoya. Most studies evaluating moyamoya after radiotherapy include to a large proportion patients with neurofibromatosis 1 (NF1), a tumor predisposition syndrome. These patients are at increased risk for moyamoya independent of radiotherapy and separate guidelines for surveillance imaging exist. After excluding these patients from otherwise eligible studies, the number of patients without moyamoya is far less than 10[60,61]. Both studies showed that radiation to the circle of Willisi or the supratentorial region is a risk factor for moyamoya. In the study from Ullrich et al., the high rate of optic pathway glioma and therefore patients with probably having NF1 might bias this observation. In the population of Wu et al., only 25% suffered from optic pathway glioma, but all received suprasellar radiotherapy. Therefore, suprasellar radiotherapy seems to be a risk factor for moyamoya.

Most WML in the reviewed literature are grade 1. In the cohort from Dietrich et al., no child with WML suffered from neurological deficits, but specific neuropsychological testing was not performed. In three studies, imaging by conventional MRI was completed by the measurement of white matter anisotropy, performed by fractional anisotropy (FA) [42,45,46]. Results show a relevant reduction of FA in selected parts of the brain in previously irradiated children compared to non-irradiated brains. There seems to be a correlation between FA-reduction and younger age at radiotherapy as well as a time span of more than 5 years after radiation. A reduced FA or white matter integrity shows a correlation with lower cognitive outcome and executive functions[42,46]. It seems that special imaging modalities (e.g. diffusion weighted imaging, measurement of

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anisotropy) are more sensitive in detection of white matter lesions than T2 weighted images alone[42]. The consequences of detected WML of any grade and the implications for therapeutic interventions are the focus of current research. We assume that early intervention, already preventive, with specific neuropsychological training help these patients to prevent the development or progression of impaired cognitive and executive functions.

The small number of studies that were eligible after we applied strict inclusion criteria, especially the limits imposed by year of diagnosis and the requirement for at least 10 patients limited our review. Since diagnoses were 1990 and onwards, the follow-up period was short, which probably biases the distribution towards more high-grade SMN and underestimates the rate of low-grade SMN. The large differences in cumulative incidence rate of vascular malformations we identified is most likely a result of small sample sizes and imaging techniques. Patients have been treated with newer modalities, so our results apply to survivors now entering follow-up care.

If a patient has strong new headache or neurological symptoms 10 years or more after treatment for a high-grade brain tumor, we recommend prompt imaging, including appropriate sequences for vascular diseases. If imaging reveals a cavernoma in a critical region, we recommend regular follow-up imaging [62]. We do not recommend surveillance imaging for small cavernoma in non-critical regions[41].

We found that screening imaging more than 10 years after completing treatment for childhood high-grade brain tumors is not indicated in absence of clinical symptoms because tumors do not

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recur after such a long period of time, and long-term sequelae (SMN, IVM, WML) occur in such a broad time spectrum that no reasonable interval for screening imaging can be defined.

Conflict of Interest Statement

There is no conflict of interest

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TABLE 1 Overview of the most important findings from the eligible studies on tumor recurrence

Study/ Year	**Trial type** **Year of diagnosis** **FU, y, median**	**Number of patients**	**Number of relapse % (n)**	**Latency from primary diagnosis to relapse, mo, median**
Medulloblastoma				
Dufour et al, 2014[11]	Single center, prospective 2001 - 2010 FU: 0.8 – 11.3 (4.4)	21	28.5% (6)	9.2 – 74.4 (19.5)
Koschmann et al, 2016[8]	Single center, retrospective 2000 - 2010 FU: 3.6 – 62.6 (18.0)	47	29.8 % (14)	3.6 – 62.6 (18.0)
Odagiri et al, 2014[12]	Single center, retrospective 2003 - 2011 FU: 1.9 – 9.1 (6.5)	16	18.7% (3)	n.a.
Perreault et al, 2013 and 2014[9,10]	Two centers, retrospective 2000 – 2011 FU: 0.23 – 11.8 (4.3)	89	29.2% (26)	0.5 – 76 (16)
Sabel et al, 2016[7]	Multicenter, prospective 2001 - 2006 FU: (7.8)	338	21% (72)	2 - 95 (26)
Sung et al, 2013[13]	Single center, prospective 2005 - 2010 FU: 1.9 – 6.8 (3.8)	20	20% (4)	6 – 21
Von Bueren at al, 2011[5]	Multicenter, prospective 2001 - 2005 FU: 1.3 – 8.2 (4.5)	45	40% (18)	2.4 – 53.9 (15.6)
Von Bueren et al, 2016[14]	Multicenter, prospective 2001 – 2007 FU: 1.2 – 9.5 (5.4)	123	38.2% (47)	SHH group: 9.6 – 16.8 (12.8) Group 3: 1.2 – 38.4 (9.6) Group 4: 4.8 – 92.4 (32.4)

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Ependymoma				
Massimio et al, 2016[18]	Multicenter, prospective 2002 - 2014 FU: 3.4 – 9.1 (5.6)	160	30.6% (49)	4 – 103 (19)
Perreault et al, 2014[9]	Two centers, retrospective 2000 – 2011 FU: 0.5 – 11.1 (3.9)	52	50% (26)	1 – 65 (16)
Rootman et al, 2017[47]	Single center, retrospective 2000 - 2015 FU: n.a.	35	54% (19)	3 – 30 (18)
Sato et al, 2017[19]	Retrospective 2000 - 2013 FU IMRT group: 1.1 – 11.7 (4.9) FU PRT group: 0.6 – 7.2 (2.6)	79	35.4% (28)	no recurrence after 5 years
Tensaouti et al, 2017[20]	Multicenter, retrospective 2000 - 2013 FU: (4.5)	202	41.6% (84)	n.a.
Venkatramani et al, 2013[48]	Prospective, multicenter 2004 - 2009 FU: (3.5)	19	47% (9)	4 – 31 (12)
Atypical teratoid rhabdoid tumor				
Bartelheim at al, 2016[24]	Multicenter, prospective 2005 - 2009 FU: 5 – 8 (6.4)	31	52% (15)	1 – 37 (6.5)
Benesch et al, 2014[25]	Multicenter, retrospective 2005 - 2011 FU : 0.6 – 6.9 (1.3)	19	74% (14)	(14)
Chi et al, 2009[26]	Multicenter, prospective 2004 – 2006 FU: up to 2.9	20	40% (8)	1.2 – 26 (5.4)

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Perreault et al, 2013 and 2014[9,10]	Two centers, retrospective 2000 – 2011 FU: 0.16 – 5.4 (0.5)	10	40% (4)	2.75 – 9 (5.5)
Sung et al, 2016[27]	Prospective 2004 – 2012 FU: 3.2 – 9 (5.3)	13	69% (9)	1 – 73 (5)
Zaky et al, 2014[28]	Prospective, multicenter 2003 – 2009 FU: n.a.	19	73% (11)	0.8 – 39.3 (4.1)
Central nervous system primitive neuroectodermal tumors (CNS-PNET), Pineoblastoma (PBL)				
Friedrich et al, 2013[30]	Multicenter, prospective 2001 - 2005 FU: 2.1 – 9.6. (8.3)	17 CNS-PNET and PBL	76% (13)	2.3 – 8.8 (5.0)
Gerber at al, 2014[31]	Multicenter, prospective 2001 - 2005 FU: 5.2 – 10.0 (7.0)	26 CNS-PNET and PBL	42% (11)	6 – 22.8 (15.6)
Perreault et al, 2013 and 2014[9,10]	Retrospective, 2 center 2000 – 2011 FU: 0.25 – 11.4 (3.7)	25 Supratentorial PNET only	56% (14)	3 – 54 (11.5)
High-grade glioma (HGG) and Diffuse intrinsic pons glioma (DIPG)				
Macy et al, 2017[35]	Prospective 2009 – 2012 FU up to 3.7	45 DIPG n=25 HGG n=20	75% (34) at 1 year	n.a.
Wolff et al, 2011[36]	Prospective 2002 - 2003	30 DIPG and HGG	EFS at 1, 2 and 5 years = 43, 20 and 13%	n.a.

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Abbreviations: CNS-PNET= central nervous system primitive neuroectodermal tumor; DIPG= diffuse intrinsic pons glioma; FU= follow-up; HGG= high grade glioma; IMRT= intensity-modulated radiation therapy; PBL= pineoblastoma; PRT= proton-beam radiation therapy; SHH= sonic hedgehog

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TABLE 2 Summary of the most important findings from the eligible studies on secondary malignant neoplasm, intracerebral vascular malformation and white matter lesion

Study/ Year	**Trial type** **Year of treatment** **FU, y, median**	**Number of patients**	**Primary tumor biology**	**Number of SMN and biology**	**Latency, y, median**
Secondary malignant neoplasm (SMN)					
Dufour et al, 2014[11]	Single center 2001 – 2010 FU: 0.8 – 11.3 (4.4)	24	MB	4.1% (1/24) - 1x HGG	After 9.3
Karremann et al, 2015[37]	Multicenter, prospective 1995 - 2007 FU: 0 – 13.8 (1.0)	1228	HGG and DIPG	0.16% (2/1228) - 1x MGM - 1x PNET	2.4 (PNET) and 10.2 (MGM)
Massimino et al, 2011[38]	Multicenter, prospective 1994 – 2003 FU: 1.2 – 15.0 (8.3)	41	EPN	2.4% (1/41) - 1x HGG	6.0
Packer et al, 2013[39]	Multicenter 1996 – 2000 FU: 0.2 – 13.7 (9.7)	379	MB	1.8% (7/379) - 6x HGG - 1x LGG	3.7 – 10.3 (6.5)
Sabel et al, 2016[7]	Multicenter, prospective 2001 – 2006 FU: (7.8)	338	MB	0.6% (2/338) - 1x DIPG - 1x HGG	5.1 (DIPG) and 4.6 (HGG)
Von Hoff et al, 2009[40]	Multicenter, prospective 1991 – 1997 FU: (10.0)	280	MB	2.1% (6/280) - 3x HGG - 2x MGM - 1x DIPG	n.a.
Intracerebral vascular malformations (IVM)					
Study/ Year	**Trial type** **Year of treatment** **FU, y, median**	**Number of patients**	**Primary tumor biology**	**Number of IVM**	**Latency, y, median**
Lew et al, 2006[41]	Single center, retrospective	59	MB	31% (18/59)	1.1 – 16.1 (6.6)

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	1996 – to present FU: 1 – 25.3 (7.2)				
Leukoencephalopathy/ White matter lesions (WML)					
Study/ Year	**Trial type** **Year of treatment** **FU, y, median**	**Number of patients**	**Primary tumor biology**	**Number of WML**	**Latency, y, median**
Brinkman et al, 2012[46]	Single center, prospective Year of treatment: n.a. FU: average 18yr	20	MB	80% (16/20) - Grade: n.a.	12 – 25 between treatment and evaluation
Dietrich et al, 2001[44]	Retrospective Year of treatment: n.a. FU: 0.5 – 15 (3.8)	44	MB n=28 EPN n=2 PNET n=5 PBL n=2 Other n=7	63.6% (28/44) - Grade I: n=13 - Grade II: n=2 - Grade III/IV: cystic n=10, hemorrhagic n=3	n.a.
Kellie et al, 2005[43]	Multicenter, retrospective 1990s FU: 4.0 – 10.5 (6.5)	12	MB n=9 PBL n=3	100% (12/12) - Grade I n=8 - Grade II n=4	4 cases with serial MRI: grade II changes in the first year; progressive WML and lacunes after 5 and 6 years
Rueckriegel et al, 2010[45]	Prospective Year of treatment: n.a. FU: (3.8)	17	MB	94% (16/17) - Grade I n=11 - Grade II n=5	n.a.

Abbreviations: DIPG= diffuse intrinsic pons glioma; EPN= ependymoma; FU= follow-up; HGG= high-grade glioma; LGG= low-grade glioma; MB= medulloblastoma; MGM= meningioma; MRI= magnetic resonance imaging; PBL= pineoblastoma; PNET= primitive neuroectodermal tumor; WML= white matter lesion